CDMRP

Department of Defense

Bone Marrow Failure Research Program





U.S. Army Medical Research and Materiel Command

Bone Marrow Failure Research Program

VISION

To understand and cure bone marrow failure disease

MISSION

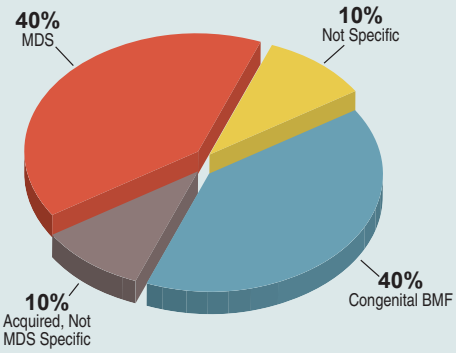
To encourage and support innovative research that is committed to advancing the understanding of inherited and acquired bone marrow failure diseases, thereby improving the health of affected individuals, with the ultimate goals of prevention and cure

Program History

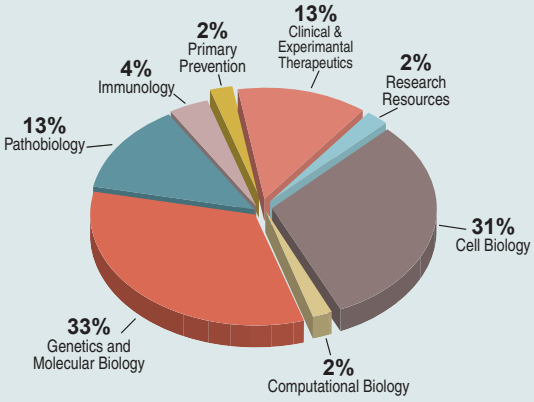
In fiscal year 2008 (FY08), the U.S. Congress appropriated $1 million (M) for bone marrow failure research. With continued appropriations, the Bone Marrow Failure Research Program (BMFRP) was established. From FY08 through FY13, $20.2M has been appropriated by Congress to research the prevention, causes, and treatment of bone marrow failure diseases. The appropriation for the FY14 BMFRP is $3.2M.

Bone marrow failure is a general term covering many different diseases. Bone marrow, the sponge-like tissue found inside bones, contains blood-forming stem cells which initiate the hematopoietic cascade for the development of all of the different cells within the blood including red blood cells, white blood cells, and platelets. Disorders affecting the stem cells or progenitor cells can, in turn, lead to bone marrow failure-rare, potentially life-threatening diseases in which the bone marrow stops functioning or produces abnormal blood cells. These diseases are classified into two major categories: acquired bone marrow failure and inherited bone marrow failure. The main objective of the BMFRP is to encourage researchers to bring their best and brightest ideas to be funded in order to enhance the field and encourage innovative thinking with ingenious solutions and paradigm-shifting findings.

Classification of BMF: Percentage of Dollars Invested



BMFRP: Percentage of Dollars Invested per Research Area



Natasha McKee, FY13 Peer Review consumer reviewer

"I thoroughly enjoyed working with the CDMRP. Everyone I interacted with was helpful and considerate plus knowledgeable and efficient. Learning more about current bone marrow failure research made me feel empowered regarding my own disease process."

BMFRP Achievements

Dr. Charles Lin demonstrated the critical role of regulatory T cells in maintaining immune privilege mechanisms of the hematopoietic stem/progenitor cells (HSPC) niche. This work has established a novel concept of immune-privilege in the HSPC niche and uncovered its molecular and cellular mechanisms.

Fujisaki J, Wu J, et al. (2011) In vivo imaging of Treg cells providing immune privilege to hematopoietic stem-cell niche. *Nature* 474: 216- 220.
http://cdmrp.army.mil/bmfrp/research_highlights/13lin_highlight.shtml

Dr. Jose Cancelas investigated the mechanism of hematopoietic stem cell (HSC) recovery after stress (ionizing radiation, chemotherapy). Deficiency in the protein connexin-43 (Cx43) highly influenced hematopoietic recovery. Results indicated that Cx43 mediates the transfer of reactive oxygen species within the bone marrow environment.

Taniguchi Ishikawa E, Gonzalez-Nieto D, et al. (2012) PNAS 109: 9071-9076; Gonzalez-Nieto D, Li L, et al. (2012) *Blood* 119: 5144-54.

Dr. Yi Zhang discovered that both Notch and Ezh2 are critical for modulating inflammatory T-cell responses that mediate graft versus host disease and bone marrow failure.

He S, Xie F, et al. (2013) The histone methyltransferase Ezh2 is a crucial epigenetic regulator of allogeneic T-cell responses mediating graft-versus-host disease. *Blood* 122: 4119-28.
http://cdmrp.army.mil/bmfrp/research_highlights/13zhang_highlight.shtml

Dr. Omar Abdel-Wahab showed that deletion of Asxl1, a protein co-factor important in epigenetic regulation of gene transcription, resulted in hallmark features of Myelodysplastic disorders (MDS), thus creating a disease-relevant genetically accurate model of MDS.

Abdel-Wahab O, Gao J, et al. (2013) Deletion of Asxl1 results in myelodysplasia and severe developmental defects in vivo. *J. Exp. Med.* 210: 2641-2659.

Martin Prager, FY13 Peer Review consumer reviewer

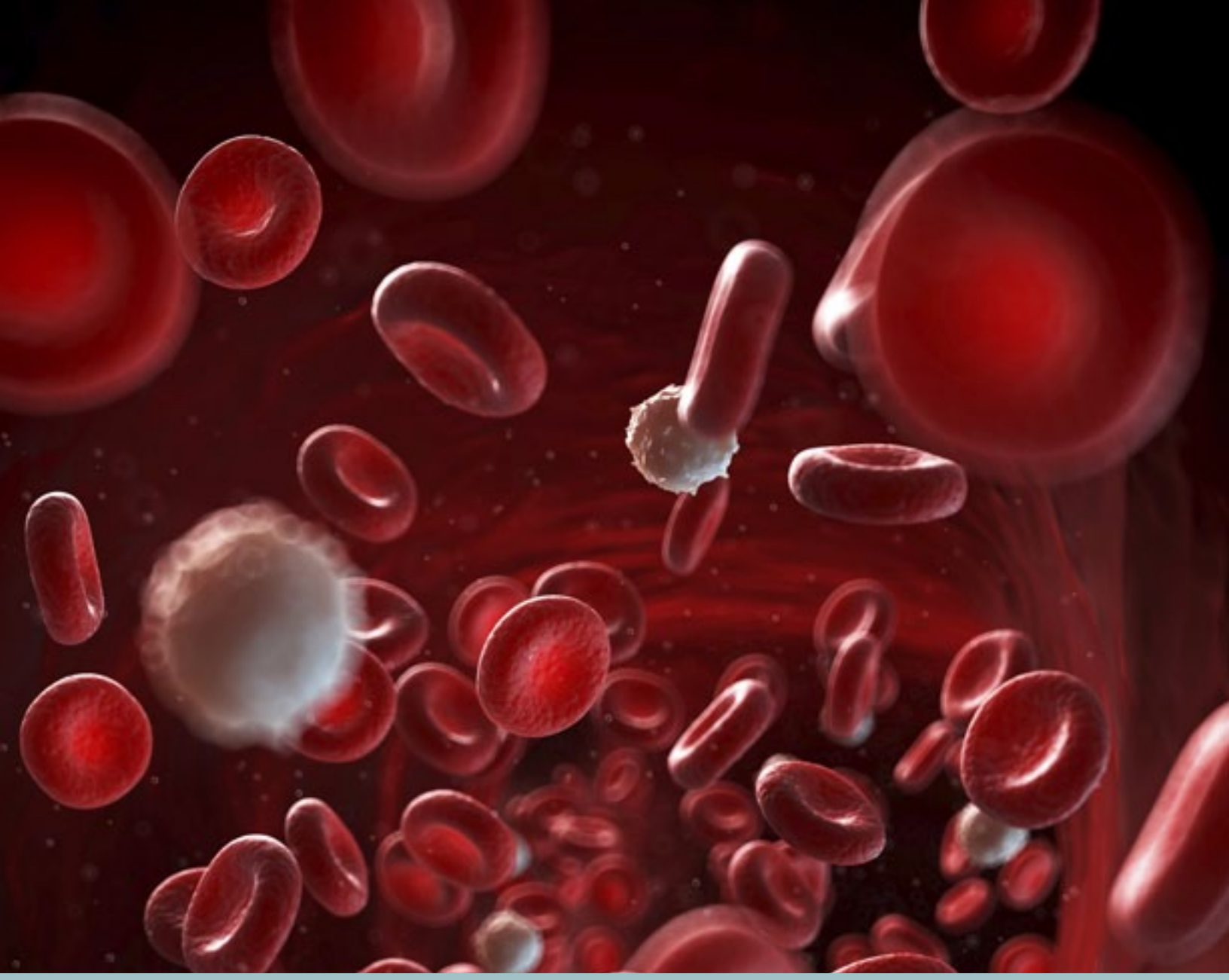
"When I experienced bone marrow failure and a subsequent successful stem cell transplant, I made an involuntary quantum leap into a new world, a parallel universe of physicians, procedures, and medicines unlike anything I ever experienced or imagined.
When I started my service as a consumer reviewer for BMFRP, it was another quantum leap into a parallel universe of genetic science populated with incredibly knowledgeable, altruistic people. The experience was both real, because I was actually part of it, and surreal in its unfamiliar terrain. The realization that I was participating in the kind of process that led ultimately, years ago, to the bone marrow transplant process we know today, was a fascinating experience and helped me appreciate my transplant even more."

Examples of inherited bone marrow failure diseases:

- Fanconi anemia
- Dyskeratosis congenital
- Shwachman-Diamond syndrome
- Diamond-Blackfan anemia

Examples of acquired bone marrow failure diseases :

- Aplastic anemia
- Myelodysplasia
- Paroxysmal nocturnal hemoglobinuria
- Pure red cell aplasia



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